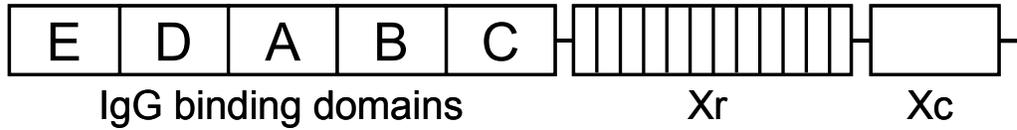


A**B****Repeat code**

7, 8, 11, 15

26

9

16, 17, 22, 23, 24, 25, 28, 31, 33

30

2, 34

19

12, 13, 20, 21

29

Repeat sequence

E	E	D	N	N	-	K	P	G
E	E	D	N	K	-	K	P	G
E	E	D	G	N	-	K	P	G
K	E	D	G	N	-	K	P	G
K	E	D	G	N	K	K	P	G
K	E	D	N	K	-	K	P	G
K	E	D	N	N	-	K	P	G
K	E	D	N	N	-	K	P	G
K	E	D	N	K	-	K	P	S

Figure S1. Protein A structure. **(A)** Domain organization in protein A. E,D,A,B,C: conserved IgG binding domains; Xr: short sequence repeat region; Xc: region of cell wall anchoring. **(B)** SSRs present in the spa types isolated with a frequency higher or equal to 1%. Protein sequences are shown and the conserved amino-acids are indicated by the black boxes.

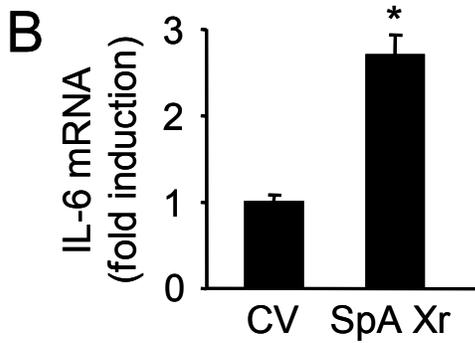
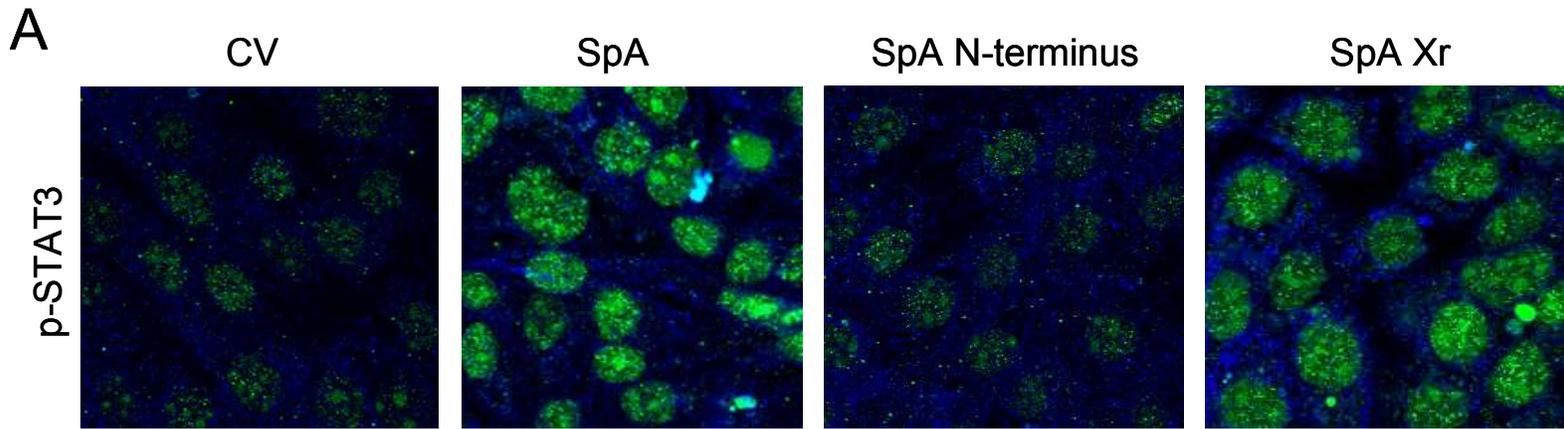


Figure S2. (A) 1HAEo-cells were transfected with a vector expressing Flag-tagged full length protein A (SpA), the IgG binding domains (SpA N-terminus) or SpA Xr. Forty eight hours later Flag expression (blue) and phospho-STAT3 (p-STAT3, green) were detected by confocal microscopy. (B) 1HAEo-cells were transfected with a vector expressing Flag-tagged SpA Xr. Forty eight hours later IL-6 induction was measured by Real Time PCR and compared to that in cells transfected with the empty vector (CV).

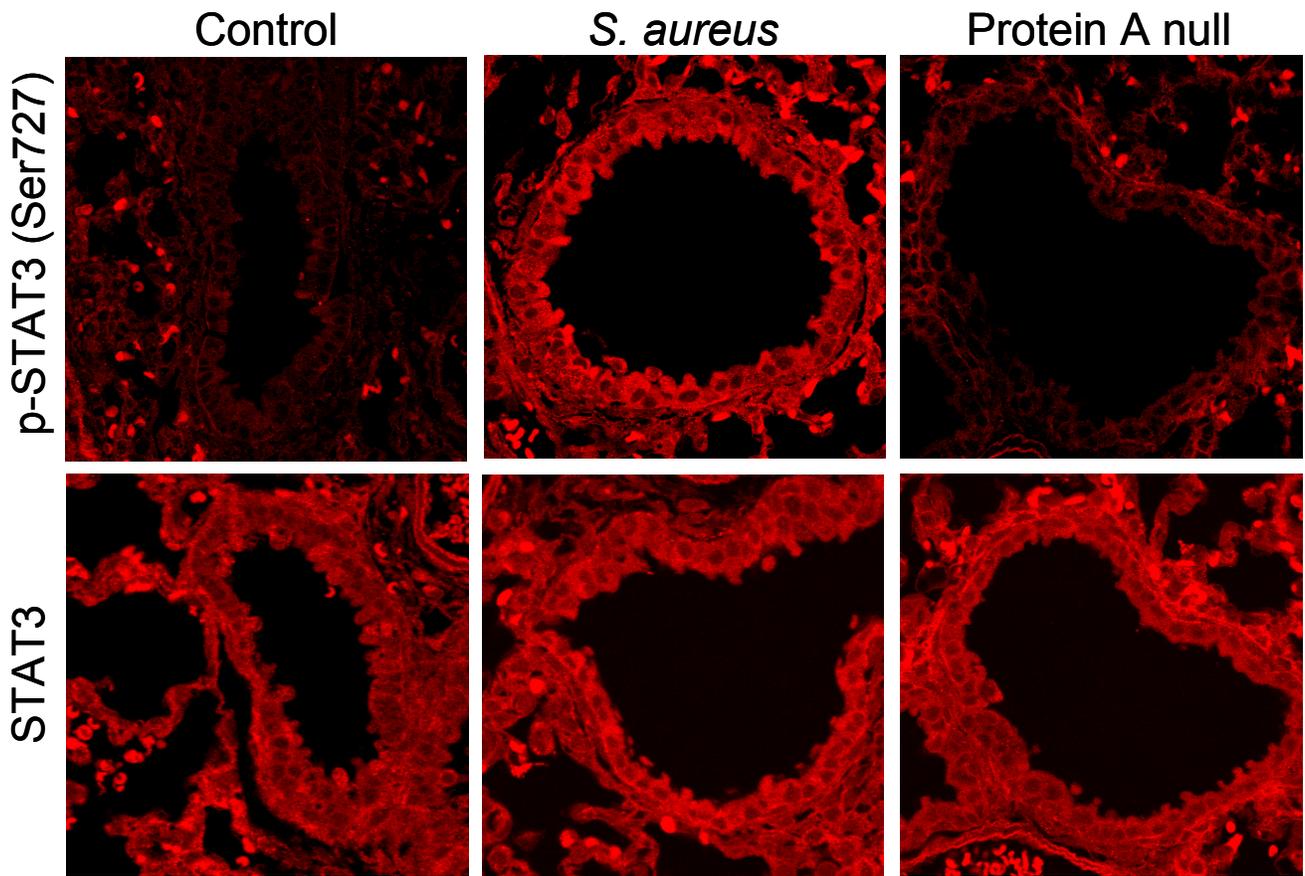


Figure S3. Phospho-STAT3 (ser 727) was detected by immunofluorescence in lung sections from control and *S. aureus* infected mice.

Table S1. Recombinant SpA Xr with different number of SSRs.

Strain	# of SSR	Repeat code	Sequence
Clinical isolate <i>spa</i> type 515	1	r07	EEDNNKPG
Clinical isolate <i>spa</i> type 131	8	r07-23-23-21-16-34-33-13	EEDNNKPG KEDGNKPG KEDGNKPG KEDNNKPG KEDGNKPG KEDNKKPG KEDGNKPG KEDNNKPG
<i>S. aureus</i> Newman	12	r07-21-21-21-21-21-23-34-34-34- 23-23	EEDNNKPG KEDNNKPG KEDNNKPG KEDNNKPG KEDNNKPG KEDNNKPG KEDGNKPG KEDNKKPG KEDNKKPG KEDNKKPG KEDGNKPG KEDGNKPG